REMARKS

I. Introduction

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

In the specification, paragraphs have been amended on pages 6, 8, 10, 16, 30, 32, 41, and 42.

Claims 46 and 47 are requested to be cancelled. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications.

Claims 27, 44, 48, 51 and 54 are currently being amended.

Claims 63-68 are being added.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Upon entry of this Amendment, claims 27-45 and 48-68 will remain pending in the application.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

II. Response to Issues Raised by Examiner in Outstanding Office Action

a. The Polypeptides Of Group I And The Polynucleotides Of Group II Exhibit Corresponding Special Technical Features

Applicants traverse the restriction requirement because the unity of invention standard must be applied in national stage applications. Section 1850 of the Manual of Patent Examining Procedure (revised 8th edition, published May, 2004) (hereinafter "MPEP") provides that

> when the Office considers international applications . . . during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111 . . . .
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> . . .
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> In applying PCT Rule 13.2 to . . . national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2 . . . .

MPEP at page 1800-94 to -95.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable . . . in national stage (filed under 35 U.S.C. 371) applications.

Id. at page 1800-199, col. 2.

According to Example 17, Part 2 of Annex B to the PCT Administrative Instructions, the Examiner is obliged to find that "the protein and the DNA sequence exhibit corresponding special technical features" and that, therefore, there is no lack of unity between claims directed to a protein "X" and the DNA sequence that encodes protein "X."

Applicants have amended claims 27, 44, 48, 51, and 54 and in the present case, unity of invention does exist between claims 27-43, 48-50, and 54-57 of Group I, which encompass polypeptides, and claims 44, 45, 48-57 of Group II, which encompass the polynucleotides which encode those polypeptides. Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to claims 27-45 and 48-57 of Groups I and II, and examine those claims in a single application.

b. Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 48-50 and 54-57 are rejected by the Examiner under 35 U.S.C. § 112, second paragraph as being allegedly indefinite because they refer to proteins. Applicants respectfully request reconsideration and withdrawal of the rejection.

Although the claims are directed to proteins, Applicants have amended claims so that Groups I and II, drawn to nucleotides and proteins, fulfill the Unity of Invention requirement, as discussed above. Therefore, claims drawn to proteins should no longer be considered a separate invention and indefinite.

The Examiner also asserts that claim 51 is indefinite because it refers to claim 27. Applicants have removed the reference to claim 27 and requests withdrawal of the rejection.

c. Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claims 44, 45, and 48-62 are rejected by the Examiner under 35 U.S.C. § 112, first paragraph. The Examiner alleges that the specification, while enabling for identification of proteins, does not reasonably provide enablement for identification and isolation of the claimed nucleic acids. In addition, the Examiner believes that the specification does not enable a person skilled in the art to make and use the invention commensurate in scope with these claims. Applicants respectfully request reconsideration and withdrawal of the rejection.

Without conceding the merits of the Examiner's rejection, but in order to expedite prosecution of the application, Applicants have amended claims 27, 44, 48, and 51 to claim those differentially expressed proteins provided in the specification. These proteins are

clearly identified in the application. For example, on pages 8-9, the specific, differentially expressed proteins are clearly identified by their corresponding name, function, and distinct "Rv"-number.

The "Rv"-number provides the person skilled in the art with clear and unambiguous support for what protein of *Mycobacterium* is described and which gene encodes the corresponding mycobacterial protein. On page 9 of the specification, Cole, et al., Nature, 393, 537-544 (1998) is disclosed (see attached). Cole describes the complete sequence of the *M. tuberculosis* H37Rv genome and identifies a total of 3924 individual genes. Table 1 of this publication provides a list of the "Rv"-classification. Furthermore, on page 543 of the Cole reference, a link to a currently active web page is given where the complete sequence of *M. tuberculosis* H37Rv could be found before the priority date of the present invention. In addition, the specification also provides a reference to web sites with the genome sequence (See page 9, second to last line, or page 16, first paragraph, lines 7-9). A person of skill in the art could have used these references to easily identify and isolate the amino acid or nucleic acid sequence from the claimed proteins. Therefore, Applicant requests withdrawal of this enablement rejection.

Claims 49, 51, 52, and 54 are rejected by the Examiner under 35 U.S.C. § 112, first paragraph. The Examiner alleges that the specification, while enabling for identification of proteins, does not reasonably provide enablement for vaccines. In addition, the Examiner believes that the specification does not enable a person skilled in the art to make and use the invention commensurate in scope with these claims. Applicants submit the declaration of Prof. Kaufmann to demonstrate that the specification provides enabling support for the claimed invention. In light of Prof. Kaufmann's declaration, and the arguments below, Applicants respectfully request reconsideration and withdrawal of the rejection.

Prof. Kaufmann's declaration describes making vaccines using the methods described in the specification. Two proteins, Rv3407 and Rv0068, are expressed in *M. tuberculosis* but not in *M. bovis* BCG, see pages 8-9 of the specification. Rv3407 and Rv0068 are representative of two types of protein variants claimed in the patent. Rv3407 is considered a

"+/- variant" (See page 8 of the specification). Rv0068 is an oxidoreductase and represents a "mobility variant" (See page 8 of the specification). The results illustrated in Prof. Kaufmann's declaration indicate that a "mobility variant" as well as a "+/- variant" are enabled as vaccines against *M. tuberculosis*.

The experiments performed by Prof. Kaufmann use protocols described in the specification and provided by the declaration. The vaccines produced from Rv0068 and Rv3407 induced protection at day 14 and day 30 post challenge (see Figures 1-2 of the declaration). Additional experiments indicate a favorable comparison between the vaccine from Rv3407 and a known vaccine (see Figure 3 of the declaration). Consistent with the protection induced by Rv3407, profound IFN-γ production and low antibody responses were observed. It is generally accepted that both CD4 and CD8 T lymphocytes are required for protective immunity against tuberculosis and with the vaccine produced from Rv3407, IFN-γ was produced by CD4 and CD8 T cells (see Figure 4 of the declaration).

The data presented in Prof. Kaufmann's declaration provides further support for the conclusion that the invention claimed in claims 49, 51, 52, and 54 are fully enabled and the rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn. In addition, new claims 63-68 relating specifically to Rv3407 and Rv0068 have been added.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant(s) hereby petition(s) for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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